REMARKS

Support for the Amendments to the Claims can be found at prior Claims 4, 10 and 40.

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DETAILED ACTION
Applicant's arguments, filed 2/18/2010, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

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Applicants have amended their claims, filed 9/8/2009, and therefore rejections newly made in the instant office action have been necessitated by amendment. Claims 4-10,19,21,23,24,28-29, and 39-47 are the current claims hereby under examination.
Claim Objections
Claim 9 is objected to because of the following informalities: Claim 9 does not appropriately end in a period. Appropriate correction is required.

The missing period has been added to Claim 9.

Claim Rejections - 35 USC § 112 First Paragraph-Modified
The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
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Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the method wherein the defined
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grouping comprises a moiety selected from the group consisting of: a specific genus, species, serotype, and another grouping below the species level, but does not reasonably provide enablement for the moiety of a tribe. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to define a grouping on the tree of relationship based on a tribe, and practice the invention commensurate in scope with these claims.
In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.
In considering the factors for the instant claims:
a) In order to practice the claimed invention one of skill in the art must make or perform the method of claim 4, specifically step O wherein one of the nodes includes tribe, i.e. a defined grouping on the tree of relationship comprises a moiety of tribe. For the reasons discussed below, undue experimentation would have been required to

practice the claimed invention.
b) The specification provides guidance for making and using a defined grouping comprising a specific genus, species, or serotype, but does not provide guidance for defining a grouping based on tribe. In other words, the specification does not provide guidance as how to go about assigning probes or establishing genetic relationships within the tree based on "tribe."
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Page 4 c)The specification does not provide any working examples of how to establish or define genetic relationships within the tree based on tribe, such as what probes to assign.
e) State of the art is complicated and unpredictable.
f) The skill of those in the art of molecular biology is high.
g) The prior art is devoid of how to divide groups genetically within a phylogenetic tree based on tribe, thus one of ordinary skill in the art would not know how to establish such genetic relationships within the tree based on race. One of skill in the art would not know how to assign or create a database of signature probes or establish genetic relationships within the tree based on tribe.
The skilled practitioner would first turn to the instant specification for guidance to practice methods of how to establish genetic relationships within the tree based on tribe. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art is devoid of such teachings. Finally, said practitioner would turn to trial and error experimentation to determine how to create such a tree of relationship based on tribe. Such represents undue experimentation.
Response to Arguments
Applicant's arguments with respect to the rejection of claim 5 under 35 USC 112 First paragraph, filed 2/18/2010 have been fully considered and are persuasive because of applicant's arguments and amendments. Therefore the rejection has been withdrawn.

Examiner Sims is thanked for withdrawing the 35 USC 112 rejection of Claim 5.

Applicant's arguments with respect to the rejection of claim 9 under 35 USC 112 First Paragraph filed 2/18/2010 have been fully considered but they are not persuasive. Applicant argues that the more narrowly define limitations in claim 9 comprising "subgroups; strain, tribe, and serotype" overcome the enablement rejection.
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Applicant's arguments are not found persuasive as defining a grouping for a "tribe" comprises the same challenge as that of race, wherein the enablement issue remains applicable.

Claim 9 has now been amended without prejudice to cancel "Tribe".

Claim Rejections - 35 USC § 112 Second Paragraph-Maintained/Modified
The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
Claims 4-10,19,21,23,24,28-29, and 39-47 and all claims dependent therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
Claim 4 and all claims dependent therefrom comprise the wording "substantially all," which has been deemed as vague and indefinite. It is unclear as to what comprises the metes and bounds of the subject matter that will be protected by the patent grant. The term "substantially all" is vague and indefinite and is not defined by the claim. Furthermore, the specification does not provide a standard for ascertaining the requisite substantially all, and one of ordinary skills in the art would not be reasonably apprised of the scope of the invention. Clarification via clearer claim

wording is required.

The objected-to word "substantially " has been cancelled from Claim 4.

Claim 28 and all claims dependent therefrom comprises a step, which is unclear
Claim 28 and all claims dependent therefrom which is unclear as to what information it provides from the "formula." In other words, the step comprises calculating a "signature quality function" using a formula, which comprises the presence of sequences in a particular group of organisms or viruses and their
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presences in other organisms NOT belonging to that group of organisms or viruses, i.e. the sequences appear to belong to any and all groups. Therefore, it is unclear as to what comprises the "single formula" and what information is derived from it when a sequence that belongs in anything and everything is included. Clarification via clearer claim wording is required.

Claim 28 has been reworded for clarification.

Response to Arguments
Applicant's arguments, filed 2/18/2010, with respect to the rejection of claim 29 under 35 USC 112 Second Paragraph have been fully considered and are persuasive because of applicant's arguments. Therefore the rejection has been withdrawn.

Examiner Sims is thanked for withdrawing the 35 USC 112 rejection of Claim 29.

Claim Rejections - 35 USC § 103-Maintained
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3.Resolving the level of ordinary skill in the pertinent art. Application/Control Number: 10/057,270
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4.Considering objective evidence present in the application indicating obviousness or nonobviousness.
5.Page 7
6.Claims 4-9,19,21,24, and 39-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al. (US PIN 6,797,817).
The claims are directed to a method for determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:
A) Obtaining or creating a nucleic acid sequence database of the same target nucleic acid, from all organisms or viruses that will be incorporated into the determination;
B) Obtaining or developing a bifurcating node phylogenetic tree having multiple nodes that establishes the genetic affinity between substantially all the organisms or viruses included in the nucleic acid sequence databases;
C) Optionally computationally fragmenting each target nucleic acid sequence such fragmentation being performed in a programmed computer so as to create a subsequence database of nucleic acid subsequences of length N that occur in at least two sequences in the nucleic acid database, where N is at least seven;

D) Tabulating in a programmed computer the extent to which the presence of each particular nucleic acid sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationship by examining the occurrence frequency of each subsequence in the target nucleic acid of the organisms and viruses encompassed by or not encompassed by each node in the tree; to create a database of characteristic signature sequences;
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E) Deriving a plurality of signature probes from a signature-database of
Page 8 characteristic signature sequences that will be complementary to a portion of the target nucleic acid sequence of the organism or virus if the signature sequence is present;
F) Hybridizing the signature probes to the target nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the target nucleic acid of the organism or virus and detecting such signals;
G) Identifying the nodes in the bifurcating node phylogenetic tree of genetic relationship that are represented by the signature probes that produced detectable signal, in order to determine the genetic affinity of the organism or virus in the test sample.
With regards to limitations of claims 4, 40, 43, and 45: Ebersole et al. teach at Col. 9, lines 35-45 that a phylogenetic Tree of Life was obtained and used for extracting sequences that represented the major microorganism domains, Bacteria and Archeae, which could be used as signature sequences for obtaining signature probes for testing for the presence of dechlorinating bacteria. Ebersole et al. further teach at the abstract, Figs. 1 - 2, and col. 5, lines 27-34, that the 16s rRNA regions, i.e. the target nucleic acid, are analyzed from the samples and organisms wherein their profiles/sequence database have been created, which reads on steps A) - B).

Ebersole *et al.* determine the sequence of 16S rRNAs from a variety of presumed dechlorinating bacteria (Col 8 lines 41-67 and Col 9 lines 1-22). "Those DNA sequences that were identified to be similar to the dechlorinating bacteria, Dehalococcoides enthenogenes" are then aligned with sequences extracted from the RDP database representing the "tree of life" (Col 9 lines 32-41). From the alignment "probable region for signature sequences were mapped" (Col 9 line 42-43). These regions are in the dechlorinating bacterium's sequence and not in the representative sequences obtained from the RDP. That is, in Ebersole *et al.* the target sequences are not the sequences of the non-dechlorinating bacteria extracted from the RDP database. In contrast, applicant's claim 4 step A and claim 40 step A specify that the sequences extracted from database of sequences are the target sequences. Thus, the sequences extracted by Ebersole *et al.* from the RDP are not used in a manner equivalent to the target sequences of the instant invention. This is further clarified by the fact Ebersole *et al.* never construct probes that target the non-dechlorinating bacteria sequences- obtained from the RDP. In contrast, it is

precisely the extracted sequences for which probes are designed in the instant invention (Claim 4 and 40 and claims dependent therefrom).

Restating the argument,- Ebersole *et al.* align the sequences of one or more dechlorinating bacteria with the extracted sequences for the purpose of identifying a "probable region for signature sequences" (col 9 Lines 43) in the sequence of each known dechlorinating bacterium not in the non-dechlorinating bacterial sequences extracted from the RDP (col 9, lines 43-50). Subsequently they find signature regions and signature sequences in the dechlorinating bacterium sequence. They never identify signature sequences in the sequences extracted from the Ribosome Database Project. In contrast, in the instant invention the extracted sequences are analyzed in order to determine the utility of all subsequences of length N in the EXTRACTED sequences, not some sequence they are aligned with. The meaning of target sequence in the applicant's claims 4 and 40 are distinctly different from the target sequences used by *Ebersole et al.* The latter are not representative of the tree of life because they can not address any taxon above that of the node containing the dechlorinating bacteria.

> *Step C) is an optional*
> *step, not necessarily performed in the instant method. However, Ebersole et al. at col. 5, lines 40-45 and col. 9, lines 11-19 and line 46 teach identifying consensus sequences, which are subsequences which occur most frequently in the 16S target*
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> *nucleic acid of the organisms from which a 16s DNA profile was created. Ebersole et al. further teach at col. 9, lines 54-56 examples of the consensus sequences wherein the sequences are of length 7 or more (see SEQ ID NO: 34), which reads on limitations of step C). Ebersole et al. further teach at col. 4, lines 55-67 and col. 5, lines 1-4, lines 40-45, col. 8, lines 1-19, col. 9, lines 11-19 and lines 54-56 using sequence analysis software in a computer to analyze the consensus sequence, wherein the consensus sequences were found in each decholorinating organism, and that the use of particular sequences, i.e. signature regions/sequences, may be used to identify decholorinators as well as for genetic sub-typing of species. In addition, Ebersole et al. at col. 5, lines 60-62 teach identifying diagnostic sequences, which are subsequences which occur in at least two other sequences in the 16S target nucleic acid of the organisms from which a 16s DNA profile was created. Ebersole et al. further teach at col. 4, examples of the diagnostic sequences wherein the sequences are of length 7 or more (see SEO ID NO:*

31 or 32), which reads on limitations of step C).

he purpose of applicant's optional step C is to remove from consideration all subsequences of length N where N is seven or more that never occur in the nucleic acid sequence database of step B. Since there are 16,384 subsequences of length seven and 262,144 of length 9, it simplifies subsequent calculations to remove from consideration those sequences that never occur in the dataset as they will always have zero signature value for all nodes. Likewise, single occurring sequences will at best only signify a single tip node. Ebersole et al. do not examine all subsequences of length N but rather instead, a modest number of consensus sequences, which differ in their very nature from the signature sequences generated by the applicant's invention. Ebersole *et al.* decreases the numbers of subsequences under consideration by selecting signature sequence regions and subsequently by constructing consensus sequences. The result is a dramatic decrease in the number of sequences considered. However, as pointed out below the process of selecting signature sequence regions may result in the overlooking of very useful sequences that occur in the region not analyzed. Because identifying signature regions with Ebersole's methods is an arbitrary manual process, it is unpredictable which sequences will be removed from consideration and unreliable in terms of finding all useful signature sequences. This especially the case for sequences that are significantly less than unique.

Ebersole et al. further teach at col. 4, lines 55-67 and col. 5, lines 1-4, lines 40-45, col. 8, lines 1-19, col. 9, lines 11-19 and lines 54-56 using sequence analysis software in a computer to analyze the consensus sequence, wherein the consensus sequences were found in each decholorinating organism, and that the use of particular sequences, i.e. signature regions/sequences, may be used to identify decholorinators as well as for genetic sub-typing of species. Furthermore, Ebersole et al. teach at col. 9, lines 46-54 that signature regions of subsequence length N (7 or more) were analyzed and found to be characteristic of different organisms, which reads on limitations of step D) and claim 45. Ebersole et al. Application/Control Number: 10/057,270

The very manner in which consensus sequences are constructed inherently requires

that only a portion of the subsequences of length N are considered. The idea behind using consensus sequences is to rapidly find subsequences that to the extent possible uniquely (Ebersole *et al.*, abstract lines 13-15; Col 8, lines 30-34; Col 9 lines 43-46; Col 18, lines 9-12) target a specific bacterial group, e.g. dechlorinating bacteria. This use of unique and nearly unique subsequences teaches away from the instant invention, which teaches instead (specification p7 lines 2-4) that sequences that are not perfect or even near perfect signatures for a specific grouping may still be useful (e.g. a Qs value of as little as 0.5 is cited in the Table on specification p. 59 as the Qs minimum). Because this is the case, the applicant's invention teaches that it is best to consider all subsequences of length N. It also should be noted that Ebersole *et al.*'s signature sequences that are used to design probes are initially obtained by examining "signature sequence regions" (Col 5 lines 34-37). Thus, "from this alignment probable region for signature sequences were mapped" Col 9 lines 40-46). Following this procedure all subsequences of length N that are not included in "signature sequence regions" or the "probable region for signature sequences" are not considered at all. Hence, the method of Ebersole *et al.* may even overlook subsequences that are in fact quite specific to a specific grouping but do not occur in a "probable region for signature sequences" Ebersole's methods for identifying useful signature sequences are clearly distinct from the methods recited in applicants claims 4, 10, and 40 and their dependent claims.

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> *teach at col. 4, lines 55-67 and col. 5, lines 1-4, that sequence profiles, from which signature probes are derived, may be used to identify and subtype bacteria with similar metabolic pathways. Therefore, a signature probe may be used to identify a dechlorinated bacteria and/or bacteria with similar metabolic pathways, such as subspecies of decholorinates, which further reads on steps E) - G).*

As pointed out previously, some dechlorinating bacteria are not in fact closely

related to *Dehalococcoides ethenogenes*. Thus, the method of Ebersole *et al.* by only using probes that distinguish members of a single grouping and possibly lower subgroupings may not succeed in proper placing of all dechlorinating bacteria. In contrast, in the applicant's invention probes to various higher groupings are also present. As a result, some knowledge of genetic affinity of a previously unencountered dechlorinating bacterium that is not related to *Dehalococcoides ethenogenes* can frequently be obtained with the applicant's invention but never with that of Ebersole *et al.* (specification Abstract lines 14-17 and p8 lines 7-10). By teaching reliance on probes to a specific taxonomic group Ebersole *et al.* fail to recognize the significant improvements that are possible by including probes to higher level taxons in the analysis. By emphasizing the value of probes to a single taxonomic group and lower groupings (but not higher groupings) Ebersole *et al.* and many others are teaching away from the instant invention that uses multiple groupings including those at higher taxonomic levels. .

Ebersole et al. at
col. 5, lines 34-39, col. 6, lines 31-34, col. 6, lines 58-67, and col. 7, lines 1-9 teach using signature sequences for generating probes and defines the use of probes and hybridization as such that is consistent in the art, which produce detectable signals, which further reads on step E). Ebersole et al. further teach at col. 2, lines 51-65, the use of signature probes in hybridizing to identify sequences such that a signal is detectable, which further reads on step F). Ebersole et al. teach at col. 8, lines 38-40 that the sequences are useful for the identification of new dechlorinating bacteria, as well as for sub-typing strains of Dehalococcoides ethenogenes. Furthermore, Ebersole et al. teach at col. 9, lines 19-40 that sequences used for obtaining probes and closest or nearest organisms to these sequences were determined, which further reads on step G).
Ebersole et al. suggest, but do not explicitly teach tabulating the extent to which the presence of each particular subsequence of length N is characteristic of each node in the bifurcating phylogenetic tree of genetic relationship by examining the occurrence frequency of each subsequence in the target nucleic acid to create a database of characteristic signature sequences. Application/Control Number: 10/057,270
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Ebersole et al. suggest this because they teach at col. 5, lines 40-45 and col. 9, lines 11-19 and lines 46-56 using software to analyze the consensus sequence, which are a set of bases which occur most often in the 16S sequences of the organisms and are characteristic of the group of decholorinating organisms. Ebersole et al. further teach determining signature regions and sequences for identifying particular organisms, which are characteristic of those organisms. sequence

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have tabulated the extent to which the presence of each particular

subsequence of length N is characteristic of each node in the bifurcating phylogenetic tree of genetic relationship by examining the occurrence frequency of each subsequence in the target nucleic acid to create a database of characteristic signature sequences in the method taught by Ebersole et al. This is because Ebersole et al. already considers how particular sequences are characteristic of individual and groups of organisms. One of skill in the art would have recognized that applying the known technique of tabulating the extent to which the sequences were characteristic of each node (i.e. group or individual organism) would have yield predictable results.

By teaching the use of "signature regions" Ebersole *et al.* are actually teaching away from the applicant's invention, which instead examines all subsequences of length N not just signature regions. The very act of identifying target regions means ignoring non-targeted regions. The discarded regions may in fact contain useful sequences and even unique or nearly unique signature sequences. Ebersole *et al.* does not suggest the applicant's method but instead teaches an approach that is distinctly different. Consistent with the argument that Ebersole's approach is fundamentally different from that of the applicant's Ebersole *et al.* utilize procedures such as sequence alignment and consensus sequence construction that are not used in the applicant's invention.

Ebersole et al. teach claims 5 and 41 -42 at col. 2, lines 50-59 wherein rDNA are used for obtaining probes, which reads on the use of DNA for comprising signature probes.
Ebersole et al. teach claim 6 at col. 6, lines 58-67 wherein hybridization is taught which is consistent in the art wherein a hybridization step is done in solution, which reads on claim 6.
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Page 12 Ebersole et al. teach claim 7 at col. 13, lines 25-30 wherein it is taught that probes which generate a detectable signal are used, which makes obvious a probe wherein the detection step utilizes radioactive labels, chemiluminescence, and/or fluorescence.

Claims 5, 6 7, 41 and 42 are distinct from Ebersole *et al.* because they are dependent on Claim 4 now amended to include Claim 10, which is distinct from Ebersole et al. as argued elsewhere herein and not rejected in the office action.

Ebersole et al. teach claim 9, of defining a grouping of a specific species, i.e. dechlorinating bacteria, see Col. 9, lines 35-45.
Ebersole et al. suggest, but do not explicitly teach wherein the tree comprises 11 or more nodes as in claim 39 and a limitation in claim 45.
Ebersole et al. suggest this because they teach at col. 1-2 a method of identifying several species of dechlorinating bacteria, which uses phylogenetic relationships.

Ebersole et al. further teach at col. 2, lines 60-65 being able to identify new strains of dechlorinating bacteria.
It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used a tree comprising 11 or more nodes for use in the method of identifying bacteria as taught by Ebersole et al. This is because Ebersole et al. teach a method of using a tree of nodes for help in identifying dechlorinating bacteria. It would have been obvious to one of ordinary skill in the art that as new/ i.e. more dechlorinating bacteria are identified, see col. 2, lines 60-65, that any phylogenetic tree used in the identification process would also comprise more nodes. Therefore, the use of 11 or more nodes in a phylogenetic tree as opposed to fewer than 11 nodes, is a result of an optimized parameter and not the product of innovation. The differences
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between the claimed invention and the prior art were encompassed in known variation or in a principal known in the prior art.

As discussed in more detail elsewhere, Ebersole *et al.* uses sequences representative of the tree of life in an alignment procedure with sequences of dechorinating bacteria in order to identify candidate regions for signature sequences. As more dechorinating bacteria are identified there is no need to increase the number of sequences from the tree of life that will be used in the alignment step. This reflects on the fact that the Tree of Life is being used in a manner which is quite distinct from that used in the instant invention.

Claim 9 and 39 are distinct from Ebersole *et al.* because they are dependent on Claim 4 now amended to include Claim 10, which is distinct from Ebersole et al. as argued elsewhere herein and not rejected in the office action.

Claim 45 is distinct from Ebersole *et al.* because it is dependent on claim 40 now amended to include Claim 10 which is distinct from Ebersole et al. as argued elsewhere herein and not rejected in the office action.

Ebersole et al. suggest, but do not explicitly teach where the same target nucleic acid sequence is obtained from at least 12 organisms or viruses as in claim 44 and a limitation of claim 45.
Ebersole et al. suggest this because they teach at col. 1-2 a method of identifying several species of dechlorinating bacteria, which uses phylogenetic relationships and several nucleic acid sequences.

Ebersole *et al.* use the tree of life to find a broad representation of sequences for their initial alignment step that is used to find probable signature sequence regions. It is not essential to their invention to know what the actual phylogenetic relationships were, only that they are representative. In fact, following sequence selection no use of the tree is made again. Likewise, as argued previously they collect data that would allow them to discover lower level phylogenetic relationships within the group of dechlorinating bacteria. However, no use of this information is made. It is simply not relevant to their invention just as sequence alignment is not relevant to the applicant's invention. In contrast, in the applicant's invention the specific phylogenetic relations are used in Claim 4 step G during the final identification process.

Claim 44 is distinct from Ebersole *et al.* because it is dependent on claim 4 now amended to include Claim 10 which is distinct from Ebersole et al. as argued elsewhere herein and not rejected in the office action.

Claim 45 is distinct from Ebersole *et al.* because it is dependent on claim 40 now amended to include Claim 10 which is distinct from Ebersole et al. as argued elsewhere herein and not rejected in the office action.

Ebersole et al. further teach at col. 2, lines 60-65 being able to identify new strains of dechlorinating bacteria. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used the same target nucleic acid sequence obtained from at least 12 organisms or viruses for use in the method of identifying bacteria as taught by Ebersole et al. This is because Ebersole et al. teach a method of using a tree of nodes for help in identifying dechlorinating bacteria. It would have been obvious to one of ordinary skill in the art that as new/ i.e. more dechlorinating bacteria are identified, see col. 2, lines 60-65, that more sequences would be used in the identification process. Therefore, the use of sequences from 12 or more organisms or viruses is a result of an optimized parameter and not the product of innovation. The differences between the claimed invention and the prior art were encompassed in known variation or in a principal known in the prior art.

As noted with respect to claim 9 above, Ebersole *et al.* use selected sequences representative of the tree of life in an alignment procedure with sequences of dechorinating bacteria in order to identify candidate regions for signature sequences. The actual phylogenetic relationship between the chosen sequences is inconsequential other than that it should provide a broad representation. As more dechorinating bacteria are identified there is no need to increase the number of sequences chosen from the tree of life for use in the alignment step. This reflects on the fact that the Tree of Life is being used in a manner, which is quite distinct from that used in the instant invention.

Claims 44 and 45 are distinct from Ebersole *et al.* because they are dependent on claim 4 now amended to include Claim 10 which is distinct from Ebersole as argued elsewhere herein and not rejected in the office action.

> *Ebersole et al at col. 9 and col. 10, teach using consensus sequences for identifying signature regions, i.e. signature sequences, wherein the sequences Application/Control Number: 10/057,270*
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>
> *Page 14 comprise at least 12 (see the 16s rONA base substitutions of the consensus sequences, which when taken independently or together are usable for a diagnostic for dechlorinating bacteria), and the consensus sequences are at least 30% identical over at least one subsequence of at least 50 nucleotides (see SEQ 10 NO: 34) as in claim 46.*
> *Ebersole et al. teach at col. 9, lines 46-65 teach using consensus sequences of length 7 or longer that occur in all the dechlorinating isolates when creating a profile, i.e. database of signature sequences as in claim 47.*
>
> *Claim 47 is dependent on claim 4 which is distinct from Ebersole et al. as argued elsewhere.*
>
> ***Response to Arguments***
> *Applicant's arguments filed 2/18/2010 have been fully considered but they are not persuasive.*
> *Applicant argues at pages 15-17 of the remarks that Ebersole does not teach a method for analyzing what is in the sample, only whether or not a particular organism or type is present.*
> *Applicant's argument is not found persuasive because Ebersole et al. teach at col. 8, lines 38-40 that the sequences are useful for the identification of new dechlorinating bacteria, as well as for sub-typing strains of Oehalococcoides*

ethenogenes, wherein the identification of new dechlorinating bacteria reads on analyzing what is in the sample and even if it has not been encountered previously, not just if an organism is present.

In instances in which Ebersole *et al.* were to detect an "unknown/new" organism it would necessarily belong to the group of dechlorinating bacteria
If it did not belong to that group, all probes would be negative and one would not even know that the organism was present let alone what it was. In contrast, the instant invention incorporates probes at multiple taxonomic levels not just that of a single species or genus (Claim 4 step E and claim 40 have been modified to emphasize this point). Thus, even in instances when the genus or species of an organism were not represented it would still be possible to (A) recognize that something unexpected is present and (B) obtain some knowledge of its taxonomic position (Gram positive vs Gram negative; Archaea vs Bacterium, etc.) would be obtained (specification p8 lines 7, p9 lines 10-17). Methods such as that of Ebersole *et al.* and others have overlooked the value of having multiple taxonomic levels represented. This is a unique and very powerful aspect of the applicant's invention.

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Page 15 Applicant argues that by seeking to determine the presence of a specific group of organisms whose identity is known ahead of time, Ebersole teach away from the present invention.
Applicant's argument is not found persuasive as Ebersole teach that "those 16S DNA gene sequences that were identified to be similar to the dechlorinating bacteria, Dehalococcoides enthenogenes DHE-195 (GenBank Accession No. AF004928), were aligned with selected 16s rRNA sequences extracted from the Ribosomal Database Project (Michigan State University) that were a representation of the major microorganism domains, Bacteria and Archeae in the Universal Phylogenetic Tree of Life. The sequences were aligned using MegAlign in DNAstar, using the default software parameters. From this alignment probable region for signature sequences were mapped. Furthermore, Ebersole teach the sequences are useful for the identification of new dechlorinating bacteria as well and therefore are not directed ONLY to specific or "known" bacteria. Further, the instant claims do not ***recite any limitations regarding whether the presence of an organisms is known (or not) prior to testing,*** *therefore the argument that Ebersole teaches away from the claimed invention is moot.*

The preamble of Claim 4 and claim 40 have been amended to include the limits of

Claim 10.

Applicant further argues at page 17 that applicant uses sequences from ALL the groupings under consideration and not an exclusive set.
Applicant's arguments are not found persuasive because Ebersole uses the Tree of Life to determine the signature properties of oligonucleotides from a dechlorinating bacteria species, wherein that specific bacteria was of interest and thus uses
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Page 16 sequences from ALL the dechlorinating bacteria species that were the target and thus were all those "incorporated into the determination" as recited in steps A and B.
Applicant further argues that Ebersole fails to recognize that sequences associated with disparate groupings can contribute to an informative result.
Applicant's arguments are not found persuasive as they are not commensurate in scope with the claimed invention. The claimed invention does not recite this limitation